=> d his

(FILE 'HOME' ENTERED AT 09:16:59 ON 28 MAR 2007)

FILE 'REGISTRY' ENTERED AT 09:17:11 ON 28 MAR 2007

E SERTRALINE (L) MANDELATE

E SERTRALINE (L) MANDELATE/CN

L1 1 S E9

FILE 'CAPLUS' ENTERED AT 09:18:10 ON 28 MAR 2007

L2 18 S L1

L3 1041 S FORM V

L4 1 S L3 AND L2

=> d bib abs 1-18 12 kwic

L2 ANSWER 1 OF 18 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2007:258084 CAPLUS

TI Sertraline acid addition salt, its preparation and its use in the preparation of sertraline hydrochloride Form II

IN Kintali, Ramana Venkata; Ludescher, Johannes; Nair, Raji; Sawant, Sudhir

PA India

SO U.S. Pat. Appl. Publ., 4pp.

CODEN: USXXCO

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
ΡI	US 2007054960	A1	20070308	US 2006-516395	20060906	
PRAI	GB 2005-18135	Α	20050906			

AB The present invention relates to novel acid addition salts of sertraline, their preparation and their use in the preparation of crystalline Form-II of Sertraline

hydrochloride.

IT 56-86-0, Glutamic acid 69-72-7, Salicylic acid 88-99-3, Phthalic acid 99-04-7, 3-Methyl benzoic acid 124-04-9, Adipic acid 611-71-2, R-Mandelic acid 7647-01-0, Hydrochloric acid 79617-96-2, Sertraline 254731-40-3

RL: RCT (Reactant); RACT (Reactant or reagent)

(sertraline acid addition salt, its preparation and its use in the preparation of

sertraline hydrochloride Form II)

- L2 ANSWER 2 OF 18 CAPLUS COPYRIGHT 2007 ACS on STN
- AN 2007:53929 CAPLUS
- DN 146:162927
- TI Process for the preparation of polymorphic crystalline sertraline hydrochloride form I and pharmaceutical dosage forms containing it
- IN Borochovitz, Ronen; Shabat, Shalom
- PA Teva Pharmaceutical Industries Ltd., Israel; Teva Pharmaceuticals Usa, Inc.
- SO PCT Int. Appl., 14pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE		
ΡI	WO 2007008317	A2	20070118	WO 2006-US22500	20060609		
	WO 2007008317	A3	20070308				

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AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
               CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
               GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR,
               KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX,
               MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD,
          MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, BU, TT, TM
               KG, KZ, MD, RU, TJ, TM
                                     20050609
PRAI US 2005-689777P
                             Ρ
     A process for the preparation of sertraline HCl form I comprises: (A) heating
      sertraline HCl in n-butanol to about 400° to about reflux temperature;
      and (B) crystallizing the sertraline HCl.
      254731-40-3, Sertraline mandelate
      RL: RCT (Reactant); RACT (Reactant or reagent)
         (process for the preparation of polymorphic crystalline sertraline
hydrochloride
         form I and pharmaceutical dosage forms containing it)
L2
      ANSWER 3 OF 18 CAPLUS COPYRIGHT 2007 ACS on STN
AN
      2006:1070265 CAPLUS
      145:397248
DN
ΤI
      Neutralization process for preparing the crystal polymorphic form II of
      sertraline hydrochloride
IN
      Ludescher, Johannes; Wieser, Josef
PA
     Austria
SO
     U.S. Pat. Appl. Publ., 4pp.
      CODEN: USXXCO
DT
      Patent
LΑ
      English
FAN.CNT 1
                                                APPLICATION NO.
      PATENT NO.
                            KIND
                                     DATE
                                                                             DATE
                                     _____
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                                                  US 2006-396967
      US 2006229472
PΙ
                             A1
                                     20061012
                                                                             20060403
PRAI GB 2005-7090
                                     20050407
      CASREACT 145:397248
os
AB
      The crystalline polymorphic form II of sertraline hydrochloride is prepared by:
      (a) providing a solution or suspension of sertraline base or one of its salts
     (e.g., sertraline mandelate) in a solvent (e.g., acetonitrile); (b) adding
      a hydrochloride of an organic amide (e.g., dimethylacetamide hydrochloride)
      at 0-120°; and (c) isolating the crystalline solid polymorphic form II
      of sertraline hydrochloride.
ΙT
      920-54-7, Dimethylacetamide hydrochloride 16889-93-3,
     N-Methylpyrrolidone hydrochloride
                                              79617-96-2, Sertraline
      254731-40-3, Sertraline mandelate
      RL: RCT (Reactant); RACT (Reactant or reagent)
         (neutralization process for preparing the crystal polymorphic form II of
         sertraline hydrochloride)
L2
     ANSWER 4 OF 18 CAPLUS COPYRIGHT 2007 ACS on STN
AN
     2006:904920 CAPLUS
DN
      145:292733
TI
     Method for preparation of the crystalline polymorphic form II of
      sertraline hydrochloride
IN
      Reguri, Buchi Reddy; Kadaboina, Rajasekhar
PΑ
      Dr. Reddy's Lab. Ltd. , India
      Indian, 21 pp.
SO
      CODEN: INXXAP
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DT Patent

LA English

FAN.CNT 1

PATENT NO. KIND APPLICATION NO. DATE DATE ---------_____ _____ IN 2000-MA765 IN 192257 20040327 20000915 PIA1 PRAI IN 2000-MA765 20000915

AB A method for the preparation of polymorphic crystalline form II of sertraline hydrochloride from any salt of Sertraline or from sertraline base comprises: (a) suspending the sertraline salt (mandelate or hydrochloride) in n-butanol, hexane, heptane, octane, nonane, cyclohexane, or their a mixts.; (b) adding an aqueous alkali solution to the suspension to obtain sertraline free base; (c) separating the aqueous layer from the biphasic mixture: (d)

optionally extracting the free base from the aqueous layer of step (c) by using a

solvent as defined in step (a) and mixing with the organic layer of step (c); (e) optionally diluting the organic layer of step (d) with n-butanol or hexane, heptane, octane, nonane, or cyclohexane; (f) acidifying the organic layer of step (e) with concentrate hydrochloric acid or gaseous hydrogen chloride or butanolic hydrogen chloride at 0-200° to obtain a sertraline hydrochloride suspension; (g) stirring the said suspension of step (f) at 0-300° for 10-36 h to obtain form II of sertraline hydrochloride in suspended form; and (h) filtering, washing, and drying the product.

IT 7647-01-0, Hydrogen chloride, reactions 254731-40-3, Sertraline mandelate

RL: RCT (Reactant); RACT (Reactant or reagent)

(in a method for preparation of the crystalline polymorphic form \mbox{II} of sertraline

hydrochloride)

- L2 ANSWER 5 OF 18 CAPLUS COPYRIGHT 2007 ACS on STN
- AN 2005:581961 CAPLUS
- DN 143:59684
- TI X-ray diffraction of a polymorph of sertraline hydrochloride
- IN Antczak, Casimir G.; Wilson, Andrew Joseph
- PA Torcan Chemical Ltd., Can.
- SO Can. Pat. Appl., 17 pp.

CODEN: CPXXEB

DT Patent

LA English

FAN CNT 1

1 2 774 · CTA	± ±						
P	ATENT NO.	KIND	DATE	APPLICATION NO.	DATE		
_							
PI C	A 2224387	A1	19990610	CA 1997-2224387	19971210		
C	A .2224387	C	20010529				
PRAI C	A 1997-2224387		19971210				
GI		,					

AB A novel polymorph of sertraline hydrochloride, i.e. (1S-cis)-4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydro-N-methyl-1-naphthalenamine hydrochloride (I·HCl), is disclosed, having improved water solubility along with acceptable stability. It is characterized by a unique x-ray diffraction pattern and unit cell structure, as well as IR and NMR spectral characteristics.

IT 254731-40-3, Sertraline mandelate
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (acid addition salt conversion; x-ray diffraction of a polymorph of sertraline hydrochloride)

L2 ANSWER 6 OF 18 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2005:474956 CAPLUS

DN 142:487606

TI Polymorphic forms of sertraline hydrochloride

PA Switz.

SO U.S. Pat. Appl. Publ., 8 pp., Cont.-in-part of U.S. Ser. No. 736,195. CODEN: USXXCO

DT Patent

LA English

FAN.CNT 3

	PA	rent :	NO.					DATE			APPL	ICAT	ION :	NO.		D	ATE	
PI		2005 2001																
		W:	AE, CR, HU, LU, SD,	AG, CU, ID, LV, SE,	AL, CZ, IL, MA, SG,	AM, DE, IN, MD,	AT, DK, IS, MG,	AU, DM, JP, MK,	AZ, DZ, KE, MN,	BA, EE, KG, MW,	BB, ES, KP, MX,	BG, FI, KR, MZ,	BR, GB, KZ, NO,	BY, GD, LC, NZ,	BZ, GE, LK, PL,	CA, GH, LR, PT,	CH, GM, LS, RO,	CN, HR, LT, RU,
		RW:	GH, DE, CF,	DK, CG,	KE, ES, CI,	FI, CM,	FR, GA,	GB,	SD, GR, GW,	IE,	IT,	LU,	MC,	NL,	PT,			-
		6872						2005	0329		US 2	002-	1119	47		2	0020	426
		2004						2004	0708		US 2	003-	7361	95		2	0031	215
	US	6939	992			B2		2005	0906									
PRAI	ΕP	1999	-810	981		Α		1999	1029									
	WO	2000	-EP1	0416		W		2000	1023									
	US	2002	-111	947		A1		2002	0426									
	US	2003	-736	195		A2		2003	1215									
OS	MAI	RPAT	142:	4876	06													

- AB An improved process for the preparation of sertraline hydrochloride polymorphic form II is described, which process comprises seeding a solution of sertraline free amine in a ketone with some crystals of polymorphic form II and addition of hydrogen chloride, and wherein the solution is heated before addition of the hydrogen chloride. According to the present process, the metastable form II may be obtained in a reliable way with good yield and high purity with respect to other polymorphic forms as well as preparative residues such as educts or solvents.
- L2 ANSWER 7 OF 18 CAPLUS COPYRIGHT 2007 ACS on STN
- AN 2004:625605 CAPLUS
- DN 143:77965
- TI Process for preparing sertraline
- IN Stohandl, Jiri; Frantisek, Jaroslav; Zapadlo, Zdenek; Stohandlova, Marta
- PA Ratiochem, S. R. O., Czech Rep.
- SO Czech Rep., 10 pp. CODEN: CZXXED
- DT Patent
- LA Czech
- FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
ΡI	CZ 292770	В6	20031217	CZ 2001-708	20010226
	BG 108940	A	20060228	BG 2004-108940	20041118
PRAI	CZ 2001-708	A	20010226	•	

- OS CASREACT 143:77965
- AB In the present invention, a process for preparing sertraline, a known antidepressant (no data), by reductive amination of a racemic 4-(3,4-dichlorophenyl)-3,4-dihydro-1(2H)naphthalenone, is disclosed. The preparation process is carried out in a single reaction vessel without isolation of intermediates. Pure cis- and trans-isomers of sertraline are separated Disclosed is also a conversion process of trans-isomer to cis-isomer, as well as preparation process of (1S)-cis-isomer polymorph.
- TT 79617-89-3P 79617-95-1P 79617-96-2P, Sertraline 79617-99-5P 254731-40-3P, Sertraline mandelate
 - RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
 - (process for preparing sertraline by reductive amination of a racemic 4-(3,4-dichlorophenyl)-3,4-dihydro-1(2H)naphthalenone)
- L2 ANSWER 8 OF 18 CAPLUS COPYRIGHT 2007 ACS on STN
- AN 2004:412910 CAPLUS
- DN 140:406641
- TI Process for the preparation of a polymorphic form of sertraline hydrochloride
- IN Nadkarni, Sunil Sadanand
- PA India
- SO PCT Int. Appl., 26 pp. CODEN: PIXXD2
- DT Patent
- DI Patent
- LA English
- FAN. CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PΙ	WO 2004041773	A1	20040521	WO 2003-IB4998	20031103
	WO 2004041773	B1	20040624		

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AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
              CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
              GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
              LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO,
              NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ,
         TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,
BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE,
ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK,
TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
     IN 2002CA00628
                            Α
                                   20040508
                                                IN 2002-CA628
                                                                         20021107
     AU 2003274608
                            A1
                                   20040607
                                                AU 2003-274608
                                                                         20031103
                                   20050803
                                                EP 2003-758583
     EP 1558561
                            A1
                                                                         20031103
             AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
              IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
                                               BR 2003-16032
                            Α
                                   20050927
                                                                         20031103
     US 2006167113
                            A1
                                   20060727
                                                US 2005-534358
                                                                         20050509
PRAI IN 2002-CA628
                            Α
                                   20021107
     WO 2003-IB4998
                            W
                                   20031103
     A process for the preparation of a polymorphic form of sertraline salts (e.g.,
AB
     sertraline hydrochloride) is described by dissolving or suspending
     sertraline mandelate in a solvent, reducing the pH of the solution or the
     suspension, and isolating the polymorphic salt of sertraline.
IT
     7647-01-0, Hydrogen chloride, reactions 254731-40-3, Sertraline
     mandelate
     RL: RCT (Reactant); RACT (Reactant or reagent)
         (in a process for the preparation of a polymorphic form of sertraline
        hydrochloride)
     ANSWER 9 OF 18 CAPLUS COPYRIGHT 2007 ACS on STN
L2
AN
     2004:340669 CAPLUS
DN
     A New and Simplified Process for Preparing N-[4-(3,4-Dichlorophenyl)-3,4-
     dihydro-1(2H)-naphthalenylidene] methanamine and a Telescoped Process for
     the Synthesis of (1S-cis)-4-(3,4-Dichlorophenol)-1,2,3,4-tetrahydro-N-
     methyl-1-naphthalenamine Mandelate: Key Intermediates in the Synthesis of
     Sertraline Hydrochloride
     Taber, Geraldine P.; Pfisterer, David M.; Colberg, Juan C.
ΑU
     Pfizer Global Research and Development, Groton, CT, 06340, USA
CS
     Organic Process Research & Development (2004), 8(3), 385-388
SO
     CODEN: OPRDFK; ISSN: 1083-6160
PΒ
     American Chemical Society
DT
     Journal
LΑ
     English
OS
     CASREACT 141:56052
AB
     N-[4-(3,4-Dichlorophenyl)-3,4-dihydro-1(2H)-naphthalenylidene]methanamine,
     sertraline imine (I), is an intermediate for the synthesis of Zoloft,
     sertraline hydrochloride. A cleaner, simpler, and more efficient
     alternative to the Schiff base-mediated formation of sertraline imine was
     developed and is presented. The condensation reaction between
     4-(3,4-dichlorophenyl)-3,4-dihydro-1(2H)-naphthalone, sertraline tetralone
     and monomethylamine was carried out in ethanol, without the need for
     classical dehydrating agent, such as TiCl4, or more novel approaches, such
     as mol. sieves, both of which produce hazardous byproducts and solid
     wastes. The low solubility of the imine I in this type of solvent is
     exploited, such that the reaction equilibrium favorably enhances the imine
     formation. Furthermore, an improved and highly selective catalytic reduction
     of I with Pd/CaCO3 catalyst in ethanol as the reaction solvent, followed
     by the resolution of the racemic cis isomer with D-(-)-mandelic acid results
     in a more efficient telescoped com. process to (1S-cis)-4-(3,4-
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dichlorophenol)-1,2,3,4-tetrahydro-N-methyl-1-naphthalen-amine mandelate,

sertraline mandelate. This new process was implemented com. and eliminates the use of hazardous material such as TiCl4, significantly reduces undesirable byproducts, reduces the number of intermediate isolations, and improves the overall process yield and productivity on industrial scale.

RE.CNT 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

IT 79560-20-6P, N-[4-(3,4-Dichlorophenyl)-3,4-dihydro-1(2H)naphthalenylidene]methanamine 254731-40-3P, (1S-cis)-4-(3,4Dichlorophenol)-1,2,3,4-tetrahydro-N-methyl-1-naphthalenamine mandelate
RL: IMF (Industrial manufacture); PREP (Preparation)

(simplified process for preparation sertraline imine and telescoped process for preparation of sertraline mandelate as key intermediates in synthesis of sertraline hydrochloride)

- L2 ANSWER 10 OF 18 CAPLUS COPYRIGHT 2007 ACS on STN
- AN 2004:101117 CAPLUS
- DN 140:163588
- TI Neutralization process for the preparation crystalline sertraline free base from sertraline salts
- IN Rao, Dharmaraj Ramachandra; Kankan, Rajendra Narayanrao; Narayan, Bhanu M.
- PA Cipla Limited, India; Wain, Christopher Paul
- SO PCT Int. Appl., 13 pp.
- CODEN: PIXXD2
- DT Patent
- LA English
- FAN.CNT 1

FAN.CNI I																			
PATENT NO.					DATE		I	APPL:	I CAT	ION	. 01		D	ATE					
						-													
	PI.	WO	2004	0114	13		A1		2004	0205	, 1	WO 20	003-0	GB31	51		20	0030	722
			W :	ΑE,	AG,	AL,	AM,	AT,	AU,	AZ,	ВÀ,	BB,	BG,	BR,	BY,	BZ,	CA,	CH,	CN,
				CO,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EC,	EE,	ES,	FI,	GB,	GD,	GE,	GH,
				GM,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	KΕ,	KG,	KR,	ΚZ,	LC,	LK,	LR,	LS,
			•	LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	MZ,	NO,	NZ,	OM,	PH,	PL,
				PT,	RO,	RU,	SC,	SD,	SE,	SG,	SK,	SL,	TJ,	TM,	TN,	TR,	TT,	TZ,	UA,
				UG,	US,	UZ,	VC,	VN,	YU,	ZA,	ZM,	zw							
			RW:	•	•	•			MZ,			•	-		-	-	-		-
				KG;	ΚZ,	MD,	RU,	TJ,	TM,	ΑT,	BE,	BG,	CH,	CY,	CZ,	DE,	DK,	EE,	ES,
				FI,	FR,	GB,	GR,	HU,	ΙE,	ΙT,	LU,	MC,	NL,	PT,	RO,	SE,	SI,	SK,	TR,
				BF,	ВJ,	CF,	CG,	CI,	CM,	GA,	GN,	GQ,	GW,	ML,	MR,	ΝE,	SN,	TD,	TG
		AU	2003	2544	75		A1		2004			_							
			2005						2005	1111		IN 20	1-200	MN45			2(J050:	117
	PRAI	GB	2002	-174	88		Α		2002	0729									
		GB	2003	-117	18		A		2003	0521									
		WO	2003	-GB3	161		W		2003	0722									
	7 D	a	7	3 2		1		e	1			- 1		2			7		- 7 -

- AB Crystalline sertraline free base is made by treating a sertraline salt (e.g., sertraline hydrochloride) with a base (e.g., aqueous NaOH) and recovering the sertraline base in crystalline form which may be used in a variety of pharmaceutical dosage form.
- RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT
- IT 79559-97-0, Sertraline hydrochloride 254731-40-3, Sertraline
 mandelate
 - RL: RCT (Reactant); RACT (Reactant or reagent)

(neutralization process for the preparation crystalline sertraline free base from $% \left(1\right) =\left(1\right) +\left(1\right) +$

sertraline salts)

- L2 ANSWER 11 OF 18 CAPLUS COPYRIGHT 2007 ACS on STN
- AN 2003:892739 CAPLUS
- DN 139:369756

English

LΑ

FAN.CNT 4

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TT
      Process for the preparation of polymorphic form II of sertraline
     hydrochloride, pharmaceutical formulations and pharmaceutical dosage forms
IN
      Borochovitch, Ronen; Mendelovici, Marioara; Nidam, Tamar; Tenengauzer,
      Ruth; Hrakovsky, Julia; Aronhime, Judith
PA
      Teva Pharmaceutical Industries Ltd., Israel; Teva Pharmaceuticals USA,
SO
      PCT Int. Appl., 30 pp.
      CODEN: PIXXD2
· DT
      Patent
T<sub>1</sub>A
      English
FAN.CNT 1
                                           APPLICATION NO.
      PATENT NO.
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                                                                  DATE
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                                          WO 2003-US13438
PΙ
     WO 2003093217
                          A1
                                 20031113
                                                                  20030429
          W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
              CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
              GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
              LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM,
              PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT,
              TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
          RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
              KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
              FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
              BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
      CA 2483569
                          A1
                                 20031113
                                             CA 2003-2483569
                                                                    20030429
     AU 2003251290
                          A1
                                 20031117
                                             AU 2003-251290
                                                                    20030429
     US 2004030190
                                             US 2003-426468
                          Α1
                                 20040212
                                                                    20030429
     US 6897340
                          B2
                                 20050524
     EP 1499581
                          A1
                                 20050126
                                            EP 2003-747621
                                                                    20030429
             AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
              IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
      US 2005209342
                          A1
                                 20050922 · US 2005-129015
                                                                    20050513
PRAI US 2002-376787P
                          Ρ
                                 20020429
     US 2003-426468
                          A1
                                 20030429
                          W
     WO 2003-US13438
                                 20030429
AB
      Processes for preparation of crystalline sertraline hydrochloride form II
      substantially free of other polymorphic forms of sertraline hydrochloride,
     preferably on an industrial scale, are presented along with X-ray
     diffraction patterns of the title crystal polymorph.
RE.CNT
               THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
              ALL CITATIONS AVAILABLE IN THE RE FORMAT
IT
      254731-40-3, Sertraline mandelate
     RL: RCT (Reactant); RACT (Reactant or reagent)
         (process for preparation of polymorphic form II of sertraline hydrochloride
         and pharmaceutical dosage forms containing it)
L2
     ANSWER 12 OF 18 CAPLUS COPYRIGHT 2007 ACS on STN
AN
     2003:585540 CAPLUS
DN
     139:138740
ΤI
     Crystallization and hydrogen chloride-neutralization methods for the
     preparation of sertraline hydrochloride crystal polymorphs
IN
     Schwartz, Eduard; Nidam, Tamar; Liberman, Anita; Mendelovici, Marioara;
     Aronhime, Judith; Singer, Claude; Valdman, Evgeni
     Teva Pharmaceutical Industries Ltd., Israel
PA
SO
     U.S., 25 pp., Cont.-in-part of U.S. 6,500,987.
     CODEN: USXXAM
DT
     Patent
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DATE

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PΙ
     US 6600073
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                                   20021231
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              CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
              PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW
         RW: GH, GM, KE, LS; MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
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              GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA,
              GN, GQ, GW, ML, MR, NE, SN, TD, TG
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              IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
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     US 2000-190603P
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                                  20000320
     CN 2001-823948
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                                  20011213
     WO 2001-US47546
                            W
                                  20011213
     US 2002-218863
                           B1
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AB
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AB Crystallization and neutralization methods for the preparation of sertraline hydrochloride crystal polymorph forms III, V, VI, VII, VII, IX, and X are presented. According to the present invention, sertraline hydrochloride Form III may be produced by heating sertraline hydrochloride Forms V and VI. Sertraline hydrochloride Forms V and VI may be produced from either sertraline hydrochloride or sertraline base by crystallization Sertraline hydrochloride Form VII may be produced by suspending sertraline hydrochloride polymorph V in water, followed by filtration. Sertraline hydrochloride Forms VIII and IX may be produced by suspending sertraline base in water followed by acidification and filtration.

RE.CNT 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

IT 254731-40-3, Sertraline mandelate

RL: RCT (Reactant); RACT (Reactant or reagent)

(crystallization and hydrogen chloride-neutralization methods for the preparation of

sertraline hydrochloride crystal polymorphs using)

NO 2004002932

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L2
    ANSWER 13 OF 18 CAPLUS COPYRIGHT 2007 ACS on STN
     2002:960678 CAPLUS
AN
DN
     138:29222
ΤI
     Preparation of sertraline hydrochloride Form II
     Schwartz, Eduard; Nidam, Tamar; Liberman, Anita; Mendelovici, Marioara;
IN
     Aronhime, Judith
PA
     Teva Pharmaceutical Industries Ltd., Israel
SO
    U.S., 9 pp., Cont.-in-part of U.S. Ser. No. 448,985.
     CODEN: USXXAM
DT
     Patent
LΑ
     English
FAN.CNT 4
     PATENT NO.
                                         APPLICATION NO.
                      KIND DATE
                                                                DATE
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                                          US 2002-218863
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                                          ZA 2004-4332
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20040712

NO 2004-2932

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PRAI US 1999-147888P
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    US 1998-110113P
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                               19981127
    US 1999-125172P
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                         Ρ
    US 1999-133117P
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    EP 1999-959091.
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    WO 2001-US47546
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                       · A1
                               20020718
    US 2002-218863
                         B1
                               20020813
    US 2004-861271
                         A1
                               20040604
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AB Sertraline hydrochloride form II may be produced directly form sertraline base or sertraline mandelate. It may also be produced from sertraline hydrochloride solvate and hydrate forms, and crystallized from new solvent systems. Pharmaceutical compns. containing sertraline hydrochloride Form II and methods of treatment using such pharmaceutical compns. are also disclosed.

RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

- L2 ANSWER 14 OF 18 CAPLUS COPYRIGHT 2007 ACS on STN.
- AN 2001:769394 CAPLUS
- DN 135:293946
- TI Sertraline and its salts for treating mammal premature ejaculation
- IN Xu, Jing
- PA Harbin Jiandi Medicine Science and Technology Development Co., Ltd., Peop. Rep. China
- SO Faming Zhuanli Shenqing Gongkai Shuomingshu, 14 pp. CODEN: CNXXEV
- DT Patent
- LA Chinese

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE		
			-,				
ΡI	CN 1285345	Α	20010228	CN 2000-124758	20000915		
	CN 1091096	В	20020918				
PRAI	CN 2000-124758		20000915				

AB Sertraline or its salt is used for treating mammal premature ejaculation. The sertraline salt is citrate, HCl, mandelate, or sulfate. The sertraline salt is prepared from mandelate by dissolving in Et acetate-water (1:1), regulating with 50% NaOH to pH 9-10, standing for 20 min, separating, extracting aqueous phase with Et acetate thrice, washing with water,

neutralizing

with citric acid, HCl, or H2SO4, crystallizing, and drying in vacuum. A tablet or capsule is prepared from sertraline citrate 54.24, Na2HPO4 10, microcryst. cellulose 25, hydroxypropyl cellulose 3, CMC-Na 4, low substituted hydroxypropyl cellulose 2.76, and Mg stearate 1%.

TT 79559-97-0, Sertraline hydrochloride 254731-40-3, Sertraline mandelate 365431-81-8 365431-84-1

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(sertraline and its salts for treating mammal premature ejaculation)

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ANSWER 15 OF 18 CAPLUS COPYRIGHT 2007 ACS on STN
L2
AN
     2001:167954 CAPLUS
DN
     134:207602
ΤI
     A reductive amination process for the preparation of cis-(1S,4S)-N-methyl-
     4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydro-1-naphthaleneamine hydrochloride
     from 4-(3,4-dichlorophenyl)-3,4-dihydro-1-(2H)-naphthalenone and
     methylamine and hydrogen
     Vyas, Sharad Kumar
IN
PA
     India
SO
     PCT Int. Appl., 23 pp.
     CODEN: PIXXD2
     Patent
DT
LΑ
     English
FAN.CNT 1
     PATENT NO.
                         KIND
                                 DATE
                                             APPLICATION NO.
                                                                     DATE
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                                           WO 2000-IB1182
     WO 2001016089
                         A:1
                                 20010308
         W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
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             HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,
             LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,
             SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN,
             YU, ZA, ZW
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ,
             CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
     IN 185109
                          A1
                                 20001118
                                             IN 1999-CA748
                                                                     19990901
PRAI IN 1999-CA748
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                                 19990901
     CASREACT 134:207602
OS
     There is disclosed a process for the preparation of
cis-(1S,4S)-N-methyl-4-(3,4-
     dichlorophenyl)-1,2,3,4-tetrahydro-1-naphthaleneamin hydrochloride (i.e.,
     sertraline hydrochloride) and the intermediate cis-N-methyl-4-(3,4-
     dichlorophenyl)-1,2,3,4-tetrahydro-1-naphthaleneamine hydrochloride, which
     comprises the reductive amination of 4-(3,4-dichlorophenyl)-3,4-dihydro-1-
     (2H) -naphthalenone with methylamine and hydrogen in the presence of a
     catalyst such as Raney Nickel to produce the intermediate amine, treating
     that amine with hydrogen chloride to produce the corresponding cis- and
     trans-amine hydrochloride salts, isolating and purifying the amine
     hydrochloride mixture to obtain the intermediate cis-amine hydrochloride,
     and converting the cis-amine hydrochloride into cis-(15,45)-N-methyl-4-
     (3,4-dichlorophenyl)-1,2,3,4-tetrahydro-1-naphthaleneamin hydrochloride.
              THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
              ALL CITATIONS AVAILABLE IN THE RE FORMAT
IT
     140631-53-4P 254731-40-3P, Sertraline mandelate
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (reductive amination process for the preparation of cis-(1S,4S)-N-methyl-4-
        (3,4-dichlorophenyl)-1,2,3,4-tetrahydro-1-naphthaleneamine
        hydrochloride from 4-(3,4-dichlorophenyl)-3,4-dihydro-1-(2H)-
        naphthalenone and methylamine and hydrogen using)
L2
     ANSWER 16 OF 18 CAPLUS COPYRIGHT 2007 ACS on STN
AN
     2000:876764 CAPLUS
DN
     134:41980
TI
     Process for preparing the (+) enantiomer of N-[4-(3,4-dichlorophenyl)-3,4-
     dihydro-1(2H)-naphthalenylidene] methanamine from the (+) enantiomer of
     4-(3,4-dichlorophenyl)-3,4-dihydro-1(2H)-naphthalenometetralone
IN
     Quallich, George Joseph
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PA Pfizer Products Inc., USA SO Eur. Pat. Appl., 11 pp. CODEN: EPXXDW

DT Patent LA English

FAN.CNT 1

PAN.	PATENT NO.	KIND DATE	APPLICATION NO.	DATE
ΡI	EP 1059287	A1 2000121	3 EP 2000-304724	20000605
	R: AT, BE, CH,	DE, DK, ES, FR	, GB, GR, IT, LI, LU, NL,	SE, MC, PT,
	IE, SI, LT,	LV, FI, RO		
	US 6593496	B1 2003071	5 US 2000-584009	20000530
	IN 186949	A1 2001121	5 IN 2000-MU503	20000531
	JP 2000351758	A 2000121	9 JP 2000-167473	20000605
	JP 3529703	B2 2004052	4	
	CA 2310799	A1 2000120	9 CA 2000-2310799	20000607
	CA 2310799	C 2004050	4	
	TR 200001657	A2 2001012	2 TR 2000-1657	20000607
	AU 767319	B2 2003110	6 AU 2000-39345	20000607
	CN 1277188	A 2000122	0 CN 2000-118079	20000608
	RU 2181358	C2 2002042	0 RU 2000-114587	20000608
	HU 200002229	A2 2002042	9 HU 2000-2229	20000608
	BR 2000002606	A 2001010	2 BR 2000-2606	20000609
PRAI	US 1999-138340P	P 1999060	9	
os	CASREACT 134:41980			
GI				

AB This invention relates to a novel improved process for preparing the (+) enantiomer of N-[4-(3,4-dichlorophenyl)-3,4-dihydro-1(2H)- naphthalenylidene]methanamine (I), an intermediate in the manufacture of sertraline, by reacting the (+) enantiomer of 4-(3,4-dichlorophenyl)-3,4-dihydro-1(2H)-naphthalenone (II) with monomethylamine and titanium chloride or mol. sieves. Subsequent I hydrogenation and salification-resolution leads to the preparation of a sertraline III salt.

RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

EP 1637516

IE, FI, CY

A1

20060322

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,

EP 2005-24398

79559-97-0P, Sertraline hydrochloride 254731-40-3P IT RL: SPN (Synthetic preparation); PREP (Preparation) (process for preparing the (+) enantiomer of N-[4-(3,4-dichlorophenyl)-3,4dihydro-1(2H)-naphthalenylidene] methanamine from the (+) enantiomer of 4-(3,4-dichlorophenyl)-3,4-dihydro-1(2H)-naphthalenonetetralone) L2 ANSWER 17 OF 18 CAPLUS COPYRIGHT 2007 ACS on STN AN 2000:384116 CAPLUS DN 133:22449 ΤI Sertraline hydrochloride polymorphs IN Schwartz, Eduard; Nidam, Tamar; Liberman, Anita; Mendelovici, Marioara; Aronheim, Jehudit; Singer, Claude; Valdman, Evgeni PA Teva Pharmaceutical Industries Ltd., Israel; Teva Pharmaceuticals Usa, Inc. SO PCT Int. Appl., 63 pp. CODEN: PIXXD2 DT Patent LΑ English FAN.CNT 4 PATENT 'NO. KIND DATE APPLICATION NO. --------------A1 WO 1999-US27881 WO 2000032551 PΙ 20000608 19991124 W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG AU 200016336 A 20000619 AU 2000-16336 19991124 EP 1133459 A1 20010919 EP 1999-959091 19991124 EP 1133459 B1 20060111 AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY JP 2002531427 Т 20020924 JP 2000-585193 19991124 AT 315544 Т 20060215 AT 1999-959091 19991124 EP 1630156 A1 20060301 EP 2005-24394 19991124 AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY EP 2005-24395 EP 1632472 A1 20060308 19991124 AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY EP 1632473 20060308 EP 2005-24396 A119991124 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY EP 1632474 Δ1 20060308 EP 2005-24400 19991124 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY EP 1632475 A1 20060308 EP 2005-24401 AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY A1 · 20060315 EP 2005-24399 AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY EP 1637515 20060322 A1 EP 2005-24397 19991124 AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY

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PRAI US 1998-110113P P
    US 2006241189
                               20061026 US 2006-415830
                                                                 20060501
                               19981127
                        P
    US 1999-125172P
                               19990319
    US 1999-133117P P
                               19990507
                    F
A3
A1
W
                            19990809
    US 1999-147888P
    EP 1999-959091
                               19991124
    US 1999-448985
                               19991124
    WO 1999-US27881
                               19991124
                        A3
    CN 2001-823948
                               20011213
    WO 2001-US47546
                        W
                               20011213
    US 2002-218863
                        B1
                               20020813
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AΒ The present invention is directed to forms II, III, V, VI, VII, VIII, IX and X of sertraline-HCl and novel methods for their preparation According to the present invention, sertraline-HCl polymorph II may be produced by slurrying sertraline-HCl polymorph VI in aprotic organic solvent. Sertraline-HCl polymorphic form III may be produced by heating sertraline-HCl polymorphs V and VI. Sertraline-HCl forms V and VI may be produced from either sertraline-HCl or sertraline base by crystallization Sertraline-HCl form VII may be produced by suspending sertraline chloride polymorph V in water, followed by filtration. Sertraline-HCl forms VIII and IX may be produced by suspending sertraline base in water followed by acidification and filtration. Sertraline-HCl form X may be produced by suspending sertraline-HCl in benzyl alc. with heating, followed by filtration. Sertraline mandelate was mixed with EtOAc and aqueous sodium hydroxide was added until the sertraline mandelate was completely neutralized. The solvent was removed under reduced pressure resulting in sertraline base as an oil. The sertraline base was dissolved in methanol and acidified with HCl until pH 1.5 was reached. The slurry was allowed to cool to room temperature and stirred for about 2 h. The solid was separated by

filtration to give sertraline-HCl methanolate-Form VI. Drying the product overnight gave sertraline-HCl form V.

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

IT 254731-40-3, Sertraline mandelate

RL: RCT (Reactant); RACT (Reactant or reagent)
 (sertraline hydrochloride polymorphs)

- L2 ANSWER 18 OF 18 CAPLUS COPYRIGHT 2007 ACS on STN
- AN 2000:59120 CAPLUS
- DN 132:93108
- TI Preparation of sertraline hydrochloride methanolate and ethanolate as antidepressants
- IN Miyamoto, Hideto; Sugi, Kiyoshi; Itaya, Nobushiqe
- PA Sumika Fine Chemicals Co., Ltd., Japan
- SO Jpn. Kokai Tokkyo Koho, 9 pp.

CODEN: JKXXAF

DT Patent LA Japanese

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
ΡI	JP 2000026379	A	20000125	JP 1998-193035	19980708	
PRAI	JP 1998-193035		19980708			

AB Sertraline (I) hydrochloride methanolate showing x-ray diffraction peaks at $2\theta=12.3$, 17.8, 22.0, 23.4, and 24.8°, and I.HCl ethanolate showing the peaks at $2\theta=12.1$, 17.5, 21.9, 22.9, and 24.2° are prepared by treatment of I with HCl (gas) in MeOH or EtOH, resp. The solvates, useful as antidepressants (no data), show high bulk d. and are filtered out in a short time unlike I.HCl.

IT 254731-40-3, Sertraline mandelate

RL: RCT (Reactant); RACT (Reactant or reagent)
 (preparation of sertraline hydrochloride methanolate or ethanolate as
 antidepressants)